August 19, 2002

Connie L. Deford
Global Environment, Health and Safety Manager
The Dow Chemical Company
2020 Dow Center
Midland, MI 48674

Dear Ms. Deford:

The Office of Pollution and Toxics is transmitting EPA's comments on the robust summaries and test plan for Chloroacetyl Chloride posted on the ChemRTK HPV Challenge Program Web site on January 23, 2002. I commend The Dow Chemical Company for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed Comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that The Dow Chemical Company advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the HPV Challenge Program Web site "Submit Technical Questions" button or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: W. Sanders
A. Abramson
C. Auer
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
Chloroacetyl Chloride

SUMMARY OF EPA COMMENTS

The Sponsor, The Dow Chemical Company, submitted a test plan and robust summaries to EPA on chloroacetyl chloride (CAS No. 79-04-9) on December 18, 2001. EPA posted the submission on the ChemRTK HPV Challenge Web site on January 23, 2002.

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical and Environmnetal Fate Data. (a) The submitter needs to indicate whether the submitted physicochemical data are measured or calculated. (b) The submitter needs to provide biodegradation, as well as transport and distribution data, for chloroacetic acid.

2. Health Endpoints. (a) The submitter needs to provide additional information to satisfy the requirements for classification of chloroacetyl chloride as a "closed system intermediate." (b) The submitter needs to consider existing published data for the genetic toxicity endpoints because mutagenicity data are inadequate and no data were submitted on chromosomal aberrations.
(c) Data on the hydrolysis product, chloroacetic acid, could be used to address/supplement a number of the health endpoints.

3. Ecological Effects. EPA agrees with the submitter that data for the hydrolysis product of chloroacetyl chloride, chloroacetic acid, can be used to satisfy the testing needs of chloroacetyl chloride for these endpoints. However, EPA reserves judgment on this aspect of the test plan until the submitter supplies robust summaries for the cited studies on chloroacetic acid.

EPA requests that the submitter advise the Agency within 60 days of any modifications to this submission.

EPA COMMENTS ON THE CHLOROACETYL CHLORIDE CHALLENGE SUBMISSION

Test Plan

Chemistry (melting point, boiling point, vapor pressure, water solubility, and partition coefficient).

The submitter needs to indicate whether the physicochemical data are measured or calculated. Measured values should be supplied. The use of estimated values introduces uncertainties that then become magnified in modeling applications.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

Due to the rapid hydrolysis of chloroacetyl chloride to chloroacetic acid, the submitter needs to include data for chloroacetic acid in its biodegradation, as well as transport and distribution, robust summaries. When developing the transport and distribution (fugacity) model for chloroacetic acid, the sponsor needs to provide the assumption and data inputs to the model (see Guidance for Robust Summary preparation). Although EPA had previously recommended the use of EQC Level I, this model is somewhat limited. EPA now recommends a level III analysis, which is more rigorous. The EQC and EPIWIN Level III models are acceptable.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

The data for the acute and repeated-dose toxicity endpoints are adequate for the purposes of the HPV Challenge Program. In addition, given the rapid hydrolysis of chloroacetyl chloride to chloroacetic acid, the submitter should utilize the data on chloroacetic acid submitted under the OECD SIDS Program when addressing the systemic health endpoints.

Genetic Toxicity. The data submitted for gene mutation are inadequate and no data were submitted for chromosome aberrations. However, published data are available that may satisfy the gene mutation and chromosome aberration endpoints (1,2). Also, the submitter needs to incorporate these data in the robust summaries.

Reproductive Toxicity. No data are available for this endpoint and no testing is proposed because of the submitter's assertion that chloroacetyl chloride is a "closed system intermediate." However, as noted above, data are available on chloroacetic acid from a 90-day study which shows no effects on male rat and mouse testes which could be used to address this endpoint.

The Guidance for Testing Closed System Intermediates for the Challenge Program at http://www.epa.gov/chemrtk/guidocs.htm allows for a reduced testing protocol provided certain criteria are met. The information required to judge a "closed system intermediate" claim must address the following:

I. Site information
   A. Number of sites.
   B. Basis for "closed process" conclusion at each site.
      1) Process description.
      2) Monitoring data showing no detection.
      3) In the absence of monitoring data, the basis for believing that releases do not occur.
   C. Data on "presence in distributed products."
II. Information on transport (mode, volume, controls, etc)
III. A data search showing that the chemical is not present in other end products.

EPA does not believe that the information provided by the submitter is adequate to satisfy the requirements for classification as a "closed system intermediate" eligible for reduced testing in the HPV Challenge Program.

The submitter states that there is another producer and an importer of chloroacetyl chloride in the U.S. The evidence is inadequate to conclude that all sites in the U.S. manufacture, process and distribute this chemical in a manner consistent with the definition of a "closed system intermediate." According to

published sources, a major use of chloroacetyl chloride is in tear gas as well as an intermediate in chemical manufacture (3,4).

For its own operations, the submitter states that chloroacetyl chloride is produced at a single facility in a completely closed system. But neither a description of the process nor a flow diagram is provided. Although the submitter provides workplace monitoring data and documentation on the mode of off-site transport, information is missing on other chemical releases or wastes generated following manufacture, documentation that the chemical is non-detectable in downstream products, volume of chemical transported to off-site customers, and information on processing and transfer by customers. A more complete description of the manufacturing process and transfer of the chemical to and from storage at each site is needed.

EPA therefore reserves judgment on whether chloroacetyl chlroide meets the criteria for a "closed system intermediate," pending the submission of additional information on the operations of the sponsor and its customers, as well as those of the other producer and the importer.

Developmental Toxicity. A developmental toxicity study is not available and is not proposed by the submitter. EPA agrees with the submitter that due to the corrosive natue of chloroacetyl chloride, conducting a developmental toxicity study would not yield meaningful results. Again, as noted above, data are available for chloroacetic acid (the sodim salt) which could be used to address this endpoint.

Ecological Effects (fish, invertebrate and algal toxicity). EPA agrees that because of the rapid conversion of chloroacetyl chloride to chloroacetic acid in aquatic media, the use of data for chloroacetic acid to address the data requirements for ecological endpoints may be acceptable, pending the submission and evaluation of appropriate robust summaries. However, the submission cannot be evaluated because the submitter did not provide summaries for the studies cited. The submitter needs to supply the robust summaries for chloroacetic acid, which will need to be updated if key data elements are missing. EPA has provided specific guidance on how to enhance the robust summaries to the standard established in EPA's HPV Challenge Program Guidance at http://www.epa.gov/chemrtk/guidocs.htm.

Specific Comments on Robust Summaries

The submitter needs to provide the purity of the test substance in Section 1.1 General Substance Information of the IUCLID Data Set.

Health Effects

Acute Toxicity. The summary for the second acute oral toxicity study is missing the following information: number and sex of animals per dose, number and sex of dead animals per dose, and number and sex of animals per dose showing clinical signs.

Repeated Dose Toxicity. The identity of the species tested are unclear. The rat is listed as the study species, but the study description lists rats, mice and hamsters. A LOAEL was reported, but it is not clear whether this LOAEL is for the rat or for all three species. Also, adverse effects on female reproductive organs (ovarian, uterine and cervical epithelial atrophy) were observed in mice in this study according to another source (5), but were not reported by the submitter. The submitter needs to clarify these issues.

Ecotoxicity

In the IUCLID Data Set submitted as robust summaries, the submitter did not provide robust summaries for

the studies cited, but referred to robust summaries for chloroacetic acid in a different IUCLID Data Set not submitted. It is the responsibility of the submitter to provide the robust summaries for the studies cited. The submitter should ensure that key data elements, such as water temperature, dissolved oxygen

content, pH, water hardness, number of organisms per test and number of replicates, are included in all robust summaries.

Follow-up Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to this submission.

References

1. American Conference of Governmental Industrial Hygienists, Inc. Documentation of the threshold limit values and biological exposure indices. 6th ed. Volumes I, II, III. 1991, Cincinnati, OH: ACGIH, p. 269.

2. Sawada M, et al. 1987, Mutat Res 187: 157-63, as reported in Hazardous Substances Data Bank. http://toxnet.nlm.nih.gov/

3. Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997, as reported in Hazardous Substances Data Bank. http://toxnet.nlm.nih.gov/

4. American Conference of Governmental Industrial Hygienists, Inc. Documentation of the threshold limit values and biological exposure indices. 6th ed. Volumes I, II, III. 1991, Cincinnati, OH: ACGIH, as reported in Hazardous Substances Data Bank. http://toxnet.nlm.nih.gov/

5. Dow Chem Co; Chloroacetyl Chloride: A Four-Week Inhalation Toxicity Study in Rats, Mice and Hamsters; 06/28/82; EPA Document No. 88-920002593S; Fiche No. OTS0536493, as reported in Hazardous Substances Data Bank. http://toxnet.nlm.nih.gov/